PATENT
Attorney Docket No. **MSU-04769**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Christoph Benning et al.

Serial No.:	09/709,020	Group No.:	1652
Filed:	11/08/00	Examiner:	Pak, Yong D

Entitled: **Compositions And Methods For The Synthesis And Subsequent Modification Of Uridine-5'-Diphosphosulfoquinovose (UDP-SQ)**

APPEAL BRIEF TRANSMITTAL

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: December 19, 2005 By: Traci E. Light

Sir or Madam:

Transmitted herewith is an Appeal Brief for this application.

1. A check in the amount of $250.00 is enclosed.

2. Please charge any additional fees, including any fees necessary for extensions of time, or credit overpayment to Deposit Account No. **08-1290**. **An originally executed duplicate of this transmittal is enclosed for this purpose.**

3. Declaration of Dr. Christoph Benning.

Dated: December 19, 2005 By: _____

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PATENT
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ATTENTION: Board of Patent Appeals and Interferences
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By: Traci E. Light

Sir or Madam:

This Brief is in furtherance of the Notice of Appeal mailed on October 19, 2005.

The fees required under § 1.17(c) are dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.

This Brief is transmitted as a single copy as per the amended rules. [37 CFR § 41.37(a).]

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This Brief contains these items under the following headings and in the order set forth below [37 CFR § 1.192(c)]

I. REAL PARTY IN INTEREST

The real party in interest is Michigan State University, 238 Administration Building East Lansing, Michigan 48824-1046.

II. RELATED APPEALS AND INTERFERENCES

There are no related applications pending appeal.

III. STATUS OF CLAIMS

1. (Appealed) A method, comprising:

a) providing:

i) uridine-5'-diphosphoglucose;

ii) sulfite;

iii) an isolated first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6; and

iv) an isolated second peptide encoded by a nucleic acid selected from the group consisting of SEQ ID NO:1 and the cDNA corresponding to SEQ ID NO:3;

b) reacting said uridine-5'-diphosphoglucose with said first peptide and said sulfite under such conditions that uridine-5'-diphosphosulfoquinovose is generated; and

c) treating said uridine-5'-diphosphosulfoquinovose with said second peptide under conditions such that sulfoquinovose diacylglycerol is generated.

2 - 12. (Canceled)

13. (Appealed) A method, comprising:

a) providing:

i) uridine-5'-diphosphoglucose;

ii) sulfite; and

iii) an isolated peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6; and

b) reacting said uridine-5'-diphosphoglucose with said peptide and said sulfur donor under such conditions that uridine-5'-diphosphosulfoquinovose is generated.

14. (Canceled)

15. (Appealed) A method, comprising:

a) providing:

i) uridine-5'-diphosphoglucose;

ii) sulfite;

iii) the nucleic acid sequence set forth in SEQ ID NO: 6; and

iv) a host cell;

b) transfecting said host cell with said nucleic acid under conditions such that a peptide is expressed;

c) isolating said expressed peptide; and

d) reacting uridine-5'-diphosphoglucose with said peptide of step (c) and said sulfite under conditions such that uridine-5'-diphosphosulfoquinovose is produced.

16. (Appealed) A method, comprising:

a) providing:

i) uridine-5'-diphosphosulfoquinovose;

ii) diacylglycerol;

iii) a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and the cDNA corresponding to SEQ ID NO:3; and

iv) a host cell

b) transfecting said host cell with said nucleic acid under conditions such that a peptide is expressed;

c) isolating said expressed peptide; and

d) reacting uridine-5'-diphosphosulfoquinovose with said peptide of step (c) and said diacylglycerol under conditions such that sulfoquinovosyl diacylglycerol produced.

17. (Appealed) A method, comprising:

a) providing:

i) a first vector comprising the nucleic acid sequence set forth in SEQ ID NO: 6;

ii) a second vector comprising the nucleic acid sequence set forth in SEQ ID NO: 1; and

iii) a host cell;

b) transfecting said host cell with first and second vectors, thereby creating a transformed host cell, under conditions such that sulfoquinovosyl diacylglycerol is produced by said transformed host cell.

18. (Appealed) The method of Claim 17, wherein said host cell, prior to said transfecting of step (b) does not produce sulfoquinovosyl diacylglycerol.

19. (Appealed) The method of Claim 18, wherein said host cell is a bacterial host cell.

20. (Appealed) The method of Claim 19, wherein said bacterial host cell is E. coli.

21. (Appealed) The method of Claim 17, wherein said first and second vectors are plasmids conferring different antibiotic resistance on said transformed host cell.

22. (Appealed) The method of Claim 17, wherein said host cell, prior to said transfecting of step (b) produces less sulfoquinovosyl diacylglycerol than said transformed host cell.

23. (Appealed) The method of Claim 22, wherein said host cell is a plant host cell.

24. (Appealed) The method of Claim 23, wherein said plant host cell is derived from a monocotyledonous plant.

25. (Appealed) The method of Claim 23, wherein said plant host cell is derived from a dicotyledonous plant.

26. (Appealed) A method, comprising:

a) providing:

i) a first vector comprising the nucleic acid sequence set forth in SEQ ID NO: 6;

ii) a second vector comprising the nucleic acid sequence corresponding to the cDNA of the sequence set forth in SEQ ID NO: 3; and

iii) a host cell;

b) transfecting said host cell with first and second vectors, thereby creating a transformed host cell, under conditions such that sulfoquinovosyl diacylglycerol is produced by said transformed host cell.

27. (Appealed) The method of Claim 26, wherein said host cell, prior to said transfecting of step (b) does not produce sulfoquinovosyl diacylglycerol.

28. (Appealed) The method of Claim 27, wherein said host cell is a bacterial host cell.

29. (Appealed) The method of Claim 28, wherein said bacterial host cell is E. coli.

30. (Appealed) The method of Claim 26, wherein said first and second vectors are plasmids conferring different antibiotic resistance on said transformed host cell.

31. (Appealed) The method of Claim 26, wherein said host cell, prior to said transfecting of step (b) produces less sulfoquinovosyl diacylglycerol than said transformed host cell.

32. (Appealed) The method of Claim 31, wherein said host cell is a plant host cell.

33. (Appealed) The method of Claim 32, wherein said plant host cell is derived from a monocotyledonous plant.

34. (Appealed) The method of Claim 32, wherein said plant host cell is derived from a dicotyledonous plant.

35. (Appealed) The method of Claim 1, further comprising the step of isolating said sulfoquinovose diacylglycerol generated in step (c).

36. (Appealed) The method of Claim 13, further comprising the step of isolating said uridine-5'-diphosphosulfoquinovose generated in step (b).

37. (Appealed) The method of Claim 15, further comprising the step of isolating said uridine-5'-diphosphosulfoquinovose produced in step (d).

38. (Appealed) The method of Claim 16, further comprising the step of isolating said sulfoquinovosyl diacylglycerol produced in step (d).

39. (Appealed) The method of Claim 17, further comprising the step of isolating said sulfoquinovosyl diacylglycerol produced in step (b).

40. (Appealed) The method of Claim 26, further comprising the step of isolating said sulfoquinovosyl diacylglycerol produced in step (b).

IV. STATUS OF AMENDMENTS

All amendments in the case have been entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention relates to methods for the synthesis and subsequent modification of uridine-5'-diphosphosulfoquinovose (UDP-SQ). Further, uridine-5'-diphosphoglucose (UDP-Glc) may be modified to create UDP-SQ that is subsequently modified to create sulfoquinovose diacylglycerol (SQDG).

In independent Claim 1, UDP-Glc is first reacted with a sulfite and an isolated first peptide (i.e., for example, an SQD1) encoded by the nucleic acid SEQ ID NO:6 to create UDP-SQ (pg 29 ln 4-26; pg 31 ln 12-16). In a second step, UDP-SQ is reacted with an isolated second peptide encoded by the nucleic acid SEQ ID NO:1 and/or the cDNA corresponding to SEQ ID NO:3 to generate SQDG (pg 33 ln 2-17). This embodiment is further defined wherein, the generated SQDG is isolated (see Claim 35; pg 34 ln 1-18).

In independent Claim 13, UDP-Glc is reacted with a sulfur donor and an isolated first peptide (i.e., for example, an SQD1) encoded by the nucleic acid SEQ ID NO:6 to create UDP-SQ (pg 29 ln 4-26; pg 31 ln 12-16). This embodiment is further defined wherein, the generated UDP-SQ is isolated (see Claim 36; pg 30 ln 1-17).

In independent Claim 15, a host cell is first transfected with the nucleic acid SEQ ID NO:6 to express the encoded peptide (pg 44 ln 1 – pg 45 ln 23). Second, the encoded peptide is isolated (pg 32 ln 1-9). Third, the isolated peptide is then reacted with UDP-Glc and a sulfite to produce UDP-SQ ((pg 29 ln 4-26; pg 31 ln 12-16)). This embodiment is further defined wherein, the generated UDP-SQ is isolated (see Claim 37; (see Claim 36; pg 30 ln 1-17)).

In independent Claim 16, a host cell is transfected with the nucleic acids SEQ ID NO:1 and/or cDNA corresponding to SEQ ID NO:3 to express the encoded protein (pg 35 ln 20 – pg 36 ln 16). Second, the encoded peptide is isolated (pg 36 ln 18-26). Third, the isolated peptide is then reacted with UDP-SQ and diacylgycerol to produce SQDG (pg 33 ln 9-17). This embodiment is further defined wherein, the generated SQDG is isolated (see Claim 38; pg 34 ln 1-18).

In independent Claim 17, a host cell is transfected with a first vector comprising SEQ ID NO:6 and a second vector comprising SEQ ID NO:1 under conditions such that SQDG is produced by the transformed cell (pg 42 ln 26 – pg 46 ln 7). This embodiment is further defined wherein, prior to transfection, the untransformed host cell either: i) does not produce sulfoquinovosyl diacylglycerol (see Claim 18); or ii) produces less sulfoquinovosyl diacylglycerol (sse Claim 22) than the transformed host cell (pg 35 ln 35 – pg 36 ln 3; pg 38 ln 1 – 5).

In independent Claim 26, a host cell is transfected with a first vector comprising SEQ ID NO:6 and a second vector comprising a nucleic acid sequence corresponding to a cDNA of the sequence set forth in SEQ ID NO:3 under conditions such that SQDG is produced by the transformed cell (pg 42 ln 26 – pg 46 ln 7). This embodiment is further defined wherein, prior to transfection, the untransformed host cell either: i) does not produce sulfoquinovosyl diacylglycerol (see Claim 27); or ii) produces less sulfoquinovosyl diacylglycerol (sse Claim 31) than the transformed host cell (pg 35 ln 35 – pg 36 ln 3; pg 38 ln 1 – 5).

VI. GROUNDS OF REJECTION TO BE REVIEWED UPON APPEAL

A. Whether Claims 1, 13, 15-22 and 35-39 are properly rejected under 35 USC § 103(a) over Benning and Essigmann et al. in view of Toth et al.

B. Whether Claims 23-25 are properly rejected under 35 USC § 103(a) over Benning and Essigmann et al. in view of Toth et al. as applied to Claims 1, 13, 15-22 and 35-39 above, and in further view of Comai et al.

C. Whether Claims 1, 13, 15-16, 26-31 and 40 are properly rejected under 35 USC § 103(a) over Benning and Essigmann et al., in view of Toth et al., in further view of Bevan et al.

D. Whether Claims 32-34 are properly rejected under 35 USC § 103(a) over Benning and Essigmann et al., and Toth et al., and Bevan et al., as applied to Claims 1, 13, 15-16, 26-31 and 40 above, and further in view of Comai et al.

VII. ARGUMENT

In summary, the Examiner has failed to show that even when using a combination of twelve references[1], not all the claim elements are taught. Specifically, the Examiner has not found any teaching that an isolated and/or expressed peptide encoded by SEQ ID NO:6 converts UDP-Glc into UDP-SQ in any of the cited references. Similarly, the Examiner has not found any teaching that an isolated and/or expressed peptide encoded by SEQ ID NO:1 and/or SEQ ID NO:3 cDNA converts UDP-SQ into SQDG in any of the cited references. In addition, the Examiner has found no relevant art with respect to transfecting cells with two vectors containing these nucleic acid sequences.

A. There Is No *Prima Facie* Case Of Obviousness

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference(s) themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Vaeck,* 947 F.2d 488, 20 USPQ.2d 1438 (Fed. Cir. 1991); and *MPEP § 2142*; Establishing A Prima Facie Case Of Obviousness. The Board is reminded that if ONLY ONE of the above requirements is not met, then a prima facie case of obviousness does not exist. The Applicants submit that the Examiner's rejections do not meet these criteria. The Applicants rebut the establishment of a *prima facie* case of obviousness by the arguments below.

As a preliminary matter, when dealing with a rejection based upon obviousness it is essential for the PTO to view the claimed embodiment as a whole:

> [T]he question under 35 U.S.C. § 103 is not whether the differences themselves would have been obvious. Consideration of differences, like each of the findings set forth in Graham, is but an aid in reaching the ultimate determination of whether the claimed invention as a whole would have been obvious.

Stratoflex Inc. v. Aeroquip Corp., 713 F.2d 1530, 1537, 218 USPQ 871 (Fed. Cir. 1983) (emphasis in the original). It is clear to the Applicants that the Examiner has not "stepped back" from the elements to actually "see" the claimed embodiment.

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[1] Only five references support 35 USC § 103(a) rejections, the other seven are allegedly "teaching" references.

Specifically, the Examiner creates numerous obviousness rejections by "picking and choosing" specific elements among the twelve (12) cited publications and subsequently uses the Applicants' specification in hindsight. The Federal Circuit has noted that:

> The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification.

In re Fritch, 972 F.2d 1260, 1266 (Fed. Cir. 1992). The Applicants note that the Examiner's conclusions allegedly establishing a *prima facie* case of obviousness are not supported by cited references. The Board is requested to note that all the Examiner's rejections rely upon Essigmann et al. and Benning. The Applicants show that Essigmann et al. and Benning represent an improper 35 USC 103(a) reference combination, thereby obviating the necessity to fully discuss each and every reference combination asserted by the Examiner.[2]

1. Rejection Under 35 USC § 103(a) Over Benning, Essigmann et al., in view of Toth et al.

a. Not All The Claim Elements Are Taught

i) Claim 1

The Examiner has ignored the Applicants' claim elements and attempts to reject the Applicants' claimed embodiment solely on the basis of protein sequences in the cited art. Claim 1 recites specific nucleic acid sequences that cannot be found in either Benning, Essigmann et al. or Toth et al. Specifically, these nucleic acid sequences comprise SEQ ID NO:1 (a first embodiment of *sqdx*), SEQ ID NO:3 (a second embodiment of *sqdx*), and SEQ ID NO: 6 (an embodiment of *sqd1*). The Examiner is not free to ignore these sequences.

Further, the Examiner admits that: "... the reference of Benning does not teach a method of producing UDP-SQ from UDP-glucose with the polypeptide encoded by SEQ ID NO:6." *Office Action Mailed 02/24/04, pg 3.* The Examiner also admits that "Essigmann et al. do not teach how to make SQDG using polypeptides encoded by

[2] The Board is reminded that the Examiner dropped combinations of: i) Essigmann et al. & Guler et al. within Office Action Mailed 05/23/02; ii) Benning, Essigmann & Guler within Office Action Mailed 07/01/03; and iii) Essigmann et al., Benning, & Punt within Office Action Mailed 02/24/04; in agreement that they did not meet 35 USC § 103(a) standards.

sqdX". *Office Action Mailed May 9, 2001 pg 8.* Toth et al. examines polyproteins which are not relevant to a biosynthetic pathway comprising *sqd1* and/or *sqdx*.[3]

The Applicants argue that the Examiner has not identified anything in Essigmann et al. that fulfills Benning's admitted deficiency relevant to the Applicants' methods. The Examiner erroneous believes that a method claim is not patentable by finding compositions indirectly related to an Applicants' claim elements within the cited references (i.e., for example, protein sequences instead of nucleic acid sequences). On the contrary, the Examiner must consider all elements within a method claim, especially those elements that are functional (i.e., for example, reacting, treating etc.). The Applicants argue that the Examiner has not fully considered the Applicants' functional claim elements.

Essigmann et al. does not teach that an isolated peptide encoded by SEQ ID NO:6 may react with UDP-Glc to produce UDP-SQ in the presence of a sulfite.[4] Similarly, Essigmann et al. does not teach that an isolated peptide encoded by SEQ ID NO:1 and/or SEQ ID NO:3 cDNA may react with UDP-SQ to produce SQDG. Further, neither Benning, Essigmann et al., nor Toth et al. suggest that any peptide encoded by SEQ ID NO:'s 1, 3, or 6 may be isolated and then reacted with a second peptide to create SQDG.

Further, the Examiner has not shown that Benning, Essigmann et al. or Toth et al. teach the isolation of sulfoquinovose diacylglycerol following its generation in an *in vitro* biochemical synthesis pathway (see Claim 35).

ii) Claim 13

The Examiner has ignored the Applicants' claim elements and attempts to reject the Applicants' claimed embodiment solely on the basis of protein sequences in the cited art. Claim 13 recites a specific nucleic acid sequence that cannot be found in either Benning, Essigmann et al. or Toth et al. Specifically, this nucleic acid sequence comprises SEQ ID NO: 6 (an embodiment of *sqd1*). The Examiner is not free to ignore this sequence. Further, the Examiner admits that: "... the reference of Benning does not teach a method of producing UDP-SQ from UDP-glucose with the polypeptide encoded by SEQ ID NO:6." *Office Action Mailed 02/24/04, pg 3.* Toth et al. examines

[3] Applicants submit that Toth et al. is non-analogous art because the Examiner has not explained how polyproteins can produce SQDG.
[4] See Claims Appendix: Declaration Of Christoph Benning filed March 11, 2002.

polyproteins which are not relevant to a biosynthetic pathway comprising *sqd1* and/or *sqdx*.[5]

The Applicants argue that the Examiner has not identified anything in Essigmann et al. that fulfills Benning's admitted deficiency relevant to the Applicants' methods. The Examiner erroneous believes that a method claim is not patentable by finding compositions indirectly related to an Applicants' claim elements within the cited references (i.e., for example, protein sequences instead of nucleic acid sequences). On the contrary, the Examiner must consider all elements within a method claim, especially those elements that are functional (i.e., for example, reacting, treating etc.). The Applicants argue that the Examiner has not fully considered the Applicants' functional claim elements. Benning, Essigmann et al., nor Toth et al. teach that an isolated peptide encoded by SEQ ID NO:6 may react with UDP-Glc to produce UDP-SQ in the presence of a sulfite.[6]

Further, the Examiner has not shown that Benning, Essigmann et al. or Toth et al. teach the isolation of uridine-5'-diphosphosulfoquinovose following its generation in an *in vitro* biochemical synthesis pathway (see Claim 36).

iii) Claim 15

The Examiner has ignored the Applicants' claim elements and attempts to reject the Applicants' claimed embodiment solely on the basis of protein sequences in the cited art. Claim 15 recites a specific nucleic acid sequences that cannot be found in either Benning, Essigmann et al., or Toth et al. Specifically, this nucleic acid sequence comprises SEQ ID NO: 6 (an embodiment of *sqd1*). The Examiner is not free to ignore this sequence.

Further, Claim 15 requires the active step of "transfecting said host cell with said nucleic acid". Neither Benning, Essigmann et al., nor Toth et al. disclose vectors comprising the above claimed nucleic acid sequence. Toth et al. examines polyproteins which are not relevant to a biosynthetic pathway comprising *sqd1* and/or *sqdx*.[7]

Without this starting material, the references: i) do not teach the requisite elements of the claim, and ii) do not enable one skilled in the art. Importantly, because of

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[5] Applicants are on record that Toth et al. is non-analogous art.
[6] See Claims Appendix: Declaration Of Christoph Benning filed March 11, 2002.
[7] Applicants are on record that Toth et al. is non-analogous art.

the degeneracy in the code, it is not possible to arrive at the nucleic acid sequence simply by looking at the amino acid sequence. This has been established in the case law. (See generally, *In re Duel* 51 F.3d 1552 (Fed. Cir. 1995); and *In re Bell*, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993)).

Further, the Examiner admits that: "... the reference of Benning does not teach a method of producing UDP-SQ from UDP-glucose with the polypeptide encoded by SEQ ID NO:6." *Office Action Mailed 02/24/04, pg 3.* The Examiner also admits that "Essigmann et al. do not teach how to make SQDG using polypeptides encoded by *sqdX*". *Office Action Mailed May 9, 2001 pg 8.*

The Applicants argue that the Examiner has not identified anything in Essigmann et al. that fulfills Benning's admitted deficiency relevant to the Applicants' methods. The Examiner erroneous believes that a method claim is not patentable by finding compositions indirectly related to an Applicants' claim elements within the cited references (i.e., for example, protein sequences instead of nucleic acid sequences). On the contrary, the Examiner must consider all elements within a method claim, especially those elements that are functional (i.e., for example, transfecting, isolating etc.). The Applicants argue that the Examiner has not fully considered the Applicants' functional claim elements.

Specifically, Essigmann et al. does not teach that an isolated peptide encoded by SEQ ID NO:6 may react with UDP-Glc to produce UDP-SQ in the presence of a sulfite.[8] Further, neither Benning, Essigmann et al., nor Toth et al. suggest that any peptide encoded by SEQ ID NO:6 may be expressed in a transfected cell, isolated, and then reacted with UDP-Glc to create UDP-SQ.

Further, the Examiner has not shown that Benning, Essigmann et al. or Toth et al. teach the isolation of uridine-5'-diphosphosulfoquinovose following its generation in an *in vitro* biochemical synthesis pathway (see Claim 37).

iv) Claim 16

The Examiner has ignored the Applicants' claim elements and attempts to reject the Applicants' claimed embodiment solely on the basis of protein sequences in the cited art. Claim 16 recites specific nucleic acid sequences that cannot be found in either

[8] See Claims Appendix: Declaration Of Christoph Benning filed March 11, 2002.

Benning, Essigmann et al., or Toth et al. Specifically, these nucleic acid sequences comprise SEQ ID NO:1 (a first embodiment of *sqdx*), and SEQ ID NO:3 (a second embodiment of *sqdx*). The Examiner is not free to ignore these sequences.

Further, Claim 16 requires the active step of "transfecting said host cell with said nucleic acid". Neither Benning, Essigmann et al., nor Toth et al. disclose vectors comprising these claimed nucleic acid sequences. Toth et al. examines polyproteins which are not relevant to a biosynthetic pathway comprising *sqd1* and/or *sqdx*.[9]

Without these starting materials, the references: i) do not teach the requisite elements of the claim, and ii) do not enable one skilled in the art. Importantly, because of the degeneracy in the code, it is not possible to arrive at the nucleic acid sequence simply by looking at the amino acid sequence. This has been established in the case law. (See generally, *In re Duel* 51 F.3d 1552 (Fed. Cir. 1995); and *In re Bell*, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993)).

The Applicants argue that the Examiner has not identified anything in Essigmann et al. that fulfills Benning's admitted deficiency relevant to the Applicants' methods. The Examiner erroneous believes that a method claim is not patentable by finding compositions indirectly related to an Applicants' claim elements within the cited references (i.e., for example, protein sequences instead of nucleic acid sequences). On the contrary, the Examiner must consider all elements within a method claim, especially those elements that are functional (i.e., for example, transfecting, isolating, reacting etc.). The Applicants argue that the Examiner has not fully considered the Applicants' functional claim elements.

Essigmann et al. does not teach that an isolated peptide encoded by SEQ ID NO:1 and/or SEQ ID NO:3 cDNA may react with UDP-SQ to produce SQDG. Further, neither Benning, Essigmann et al., nor Toth et al. suggest that any peptide encoded by SEQ ID NO:'s 1 or 3 may be expressed in a transfected cell, isolated, and then reacted with a second peptide to create SQDG.

Further, the Examiner has not shown that Benning, Essigmann et al. or Toth et al. teach the isolation of sulfoquinovose diacylglycerol following its generation in an *in vitro* biochemical synthesis pathway (see Claim 38).

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[9] Applicants are on record that Toth et al. is non-analogous art.

v) Claim 17

The Examiner has ignored the Applicants' claim elements and attempts to reject the Applicants' claimed embodiment solely on the basis of protein sequences in the cited art. Claim 17 recites specific nucleic acid sequences that cannot be found in either Benning, Essigmann et al., or Toth et al. Specifically, these nucleic acid sequences comprise SEQ ID NO:1 (a first embodiment of *sqdx*), and SEQ ID NO: 6 (an embodiment of *sqd1*). The Examiner is not free to ignore these sequences.

Further, Claim 17 requires "transfecting said host cell with first and second vectors". Neither Benning, Essigmann et al., nor Toth et al. disclose vectors comprising all the claimed nucleic acid sequences. Toth et al. examines polyproteins which are not relevant to a biosynthetic pathway comprising *sqd1* and/or *sqdx*.[10]

Without these starting materials, the references: i) do not teach the requisite elements of the claim, and ii) do not enable one skilled in the art. Importantly, because of the degeneracy in the code, it is not possible to arrive at the nucleic acid sequence simply by looking at the amino acid sequence. This has been established in the case law. (See generally, *In re Duel* 51 F.3d 1552 (Fed. Cir. 1995); and *In re Bell*, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993)).

The Applicants argue that the Examiner has not identified anything in Essigmann et al. that fulfills Benning's admitted deficiency relevant to the Applicants' methods. The Examiner erroneous believes that a method claim is not patentable by finding compositions indirectly related to an Applicants' claim elements within the cited references (i.e., for example, protein sequences instead of nucleic acid sequences). On the contrary, the Examiner must consider all elements within a method claim, especially those elements that are functional (i.e., for example, transfecting, creating etc.). The Applicants argue that the Examiner has not fully considered the Applicants' functional claim elements.

Neither Benning, Essigmann, nor Toth et al suggest that peptides encoded by SEQ ID NO:'s 1 or 6 may be co-expressed in a transfected cell to create SQDG.

[10] Applicants are on record that Toth et al. is non-analogous art.

Further, the Examiner has not shown that Benning, Essigmann et al. or Toth et al. teach the isolation of sulfoquinovose diacylglycerol following its generation in an *in vitro* biochemical synthesis pathway (see Claim 39).

b. There Is No Motivation To Combine The Art

The Examiner makes a failed attempt to show a motivation to modify Benning with Essigmann et al. and Toth et al.:

> Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to substitute the first reaction of SQDG synthesis of Benning with the SQD1 enzyme of Essigmann et al. [s]ince the SQD1 gene and the bacterial sqdB gene are the only sulfolipid genes known to be conserved between different organisms [11], one of ordinary skill in the art would have been motivated to interchange the two enzyme[s] ...

Office Action Mailed 07/01/03 pg 4. The Federal Circuit has made it very clear that motivations to modify the art must come from the cited references themselves.[12] Neither Benning, Essigmann et al., nor Toth et al. provide any teaching that the SQD1 should be interchanged with the sqdB gene. The Examiner made this realization by reading the Applicant's specification, thereby resulting in impermissible hindsight[13]. The Examiner has merely proffered personal opinion to make a leap of unsupported logic. An Examiner is NOT one skilled in the art; mere opinion of the Examiner on what one skilled in the art might believe does not count. *In re Rijckaert*, 9 F.3d 1531, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993) ("[T]he examiner's assumptions do not constitute the disclosure of the prior art.").

The Examiner offers other personal opinions, for example:

> Essigmann et al. teach that SQD1 catalyzes formation of UDP-sulfoquinovose from UDP and a sulfur donor and Guler et al. teach that SQDX catalyzes the formation of SQDG from UDP-sulfoquinovose.

Office Action Mailed 11/26/01 pg 6. The Applicants disagree and point out that neither Essigmann et al. nor Guler et al. suggest that their pathways should, or could, be modified with the other. For example, Essigmann et al. does not suggest that the formation of UDP-SQ by SQD1 should be modified to include the formation of SQDG

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[11] The Applicants' fail to understand the significance of this statement.

[12] "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification. *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992)

[13] *W. L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1550, 220 USPQ 303, 311 (Fed. Cir. 1983).

by sqdX. Vice versa, Guler et al. does not suggest that the formation of SQDG by *sqdX* should be modified to include the formation of UDP-SQ by *SQD1*. As the Applicants' have argued repeatedly, the Examiner has never pointed to any statements within any reference to suggest any modification to create the Applicants' claimed embodiment.

c. There Is No Expectation Of Success

A proper analysis under 35 U.S.C. § 103(a) requires that a combination of references must provide a reasonable expectation of success should the claimed combination be carried out. *MPEP* § 2143.02. Moreover, "both the suggestion and reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck,* 20 USPQ.2d 1438, 1442, 947 F.2d 488 (Fed. Cir. 1991). Essigmann et al., when read in view of teaching reference Guler et al. (as suggested by the Examiner) both do not provide any explicit suggestions that the Applicants' claimed embodiment would, in fact, work[14]. The same is true for both Benning and Toth et al.

The Examiner, instead, simply offers personal interpretations of passages within the cited art in order to "fabricate an expectation of success", for example:

> One of ordinary skill in the art would have had a reasonable expectation of success since Essigmann et al. outlines the pathway for SQDG production and production of a product using recombinant enzymes in lieu of chemical synthesis is routinely performed.

Final Office Action Mailed Nov.26, 2001.

The Examiner also fails to reflect Guler's prophetic context, for example:

> Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to make SQDG with the polypeptide encoded by *sqdX* of Guler et al.

Office Action Mailed 05/09/01 pg 8 and Final Office Action Mailed 11/26/01, pg 3. In making this conclusion, the Examiner ignores the underlined hypothetical context from the relied upon passage:

> ... *SQDG1* ... genes encode highly conserved proteins with similarity to sugar-nucleotide-modifying enzymes which <u>are proposed</u> to be involved in the biosynthesis of the UDP-sulfoquinovose headgroup donor for sulfolipid biosynthesis ... [and] ... *sqdX*... sequence similarity to glycosyltransferases strongly suggests that *sqdX* encodes the sulfolipid synthase catalyzing the transfer of sulfoquinovose from UDP-sulfoquinovose onto a suitable acceptor, <u>presumably</u> diacylglycerol.

[14] The expectation of success must come from the prior art and explicitly predict that the process recited in the claims would work. *In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988).

Guler et al., pg 545 ¶ 1 [emphasis added]. Guler et al. is clearly speculating and, as such, must be interpreted as "obvious to try" which does not rise to the statutory level of 35 U.S.C. § 103(a)[15]. Since an expectation of success is required to be explicitly present in a cited reference the Examiner's argument fails.

2. Rejection Under 35 USC § 103(a) Over Benning, Essigmann et al., in view of Toth et al., and in further view of Comai et al.

The Applicants request that all arguments presented in Section VII(A)(1)(a)(v), Section VII(A)(1)(b) and Section VII(A)(1)(c) be herein incorporated by reference. Further, as discussed below Comai et al. adds nothing to fill the deficiencies of Benning, Essigmann et al. and Toth et al. identified above. Specifically, Comai et al. discloses no nucleic acid sequences and is limited to plasmids containing a CaMV 35S-enhanced mannopine synthase promoter. Consequently, Claims 23-25 are not obvious because the independent Claim 17 is not obvious.

3. Rejection Under 35 USC § 103(a) Over Benning and Essigmann et al., in view of Toth et al. in further view of Bevan et al.

a. Not All The Claim Limitations Are Taught

i) Claim 1

The arguments within Section VII(A)(1)(a)(i) are herein incorporated by reference. Bevan et al. presents merely a nucleotide sequence and does not add any teachings relevant to an isolated biosynthetic pathway comprising SEQ ID NO:6, 3, or 1.

ii) Claim 13

The arguments within Section VII(A)(1)(a)(ii) are herein incorporated by reference. Bevan et al. presents merely a nucleotide sequence and does not add any teachings relevant to an isolated biosynthetic pathway comprising SEQ ID NO:6.

iii) Claim 15

The arguments within Section VII(A)(1)(a)(iii) are herein incorporated by reference. Bevan et al. presents merely a nucleotide sequence and does not add any teachings relevant to transfecting a host cell with a nucleic acid comprising SEQ ID NO:6.

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[15] "Of course, an 'obvious to try' standard is not a legitimate test of patentability." *American Hospital Supply Corp. v. Travenol Laboratories, Inc.*, 745 F.2d 1, 223 USPQ 577 (Fed. Cir. 1984)

iv) Claim 16

The arguments within Section VII(A)(1)(a)(iv) are herein incorporated by reference. Bevan et al. presents merely a nucleotide sequence and does not add any teachings relevant to transfecting a host cell with nucleic acids comprising SEQ ID NO:1 or 3.

v) Claim 26

The Examiner has ignored the Applicants' claim elements and attempts to reject the Applicants' claimed embodiment solely on the basis of protein sequences in the cited art. Claim 26 recites specific nucleic acid sequences that cannot be found in either Benning, Essigmann et al., or Toth et al. Specifically, these nucleic acid sequences comprise SEQ ID NO:3 (a second embodiment of *sqdx*), and SEQ ID NO: 6 (an embodiment of *sqd1*). The Examiner is not free to ignore these sequences. Further, Claim 26 requires "transfecting said host cell with first and second vectors". Neither Benning, Essigmann et al., Toth et al., nor Bevan et al. disclose vectors comprising all the claimed nucleic acid sequences. Bevan et al. is presented only for disclosure of a nucleic acid sequence, but as an EMBL database entry, there is no teachings or disclosure as to how to make and use the disclosed nucleic acid sequence. Without these starting materials, the references: i) do not teach the requisite elements of the claim, and ii) do not enable one skilled in the art. Importantly, because of the degeneracy in the code, it is not possible to arrive at the nucleic acid sequence simply by looking at the amino acid sequence. This has been established in the case law. (See generally, *In re Duel* 51 F.3d 1552 (Fed. Cir. 1995); and *In re Bell*, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993)).

The Applicants argue that the Examiner has not identified anything in Essigmann et al. that fulfills Benning's admitted deficiency relevant to the Applicants' methods. The Examiner erroneous believes that a method claim is not patentable by finding compositions indirectly related to an Applicants' claim elements within the cited references (i.e., for example, protein sequences instead of nucleic acid sequences). On the contrary, the Examiner must consider all elements within a method claim, especially those elements that are functional (i.e., for example, transfecting, creating etc.). The Applicants argue that the Examiner has not fully considered the Applicants' functional claim elements.

Neither Benning, Essigmann, Toth et al., nor Bevan et al. suggest that peptides encoded by SEQ ID NO:'s 3 or 6 may be co-expressed in a transfected cell to create SQDG.

Further, the Examiner has not shown that Benning, Essigmann et al., Toth et al. or Bevan et al. teach the isolation of sulfoquinovose diacylglycerol following its generation in an *in vitro* biochemical synthesis pathway (see Claim 40).

b. There Is No Motivation To Combine The Art

The Examiner makes a failed attempt to show a motivation to modify Benning with Essigmann et al., Toth et al., and Bevan et al.:

> Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to substitute the first reaction of SQDG synthesis of Benning with the SQD1 enzyme of Essigmann et al. [s]ince the SQD1 gene and the bacterial sqdB gene are the only sulfolipid genes known to be conserved between different organisms [16], one of ordinary skill in the art would have been motivated to interchange the two enzyme[s] ...

Office Action Mailed 07/01/03 pg 4. The Federal Circuit has made it very clear that motivations to modify the art must come from the cited references themselves.[17] Neither Benning, Essigmann et al., Toth et al., nor Bevan et al. provide any teaching that the SQD1 should be interchanged with the sqdB gene. The Examiner made this realization by reading the Applicant's specification, thereby resulting in impermissible hindsight[18]. The Examiner has merely proffered personal opinion to make a leap of unsupported logic. An Examiner is NOT one skilled in the art; mere opinion of the Examiner on what one skilled in the art might believe does not count. *In re Rijckaert*, 9 F.3d 1531, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993) ("[T]he examiner's assumptions do not constitute the disclosure of the prior art.").

The Examiner offers other personal opinions, for example:

> Essigmann et al. teach that SQD1 catalyzes formation of UDP-sulfoquinovose from UDP and a sulfur donor and Guler et al. teach that SQDX catalyzes the formation of SQDG from UDP-sulfoquinovose.

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[16] The Applicants' fail to understand the significance of this statement.

[17] "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification. *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992)

[18] *W. L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1550, 220 USPQ 303, 311 (Fed. Cir. 1983).

Office Action Mailed 11/26/01 pg 6. The Applicants disagree and point out that neither Essigmann et al. nor Guler et al. suggest that their pathways should, or could, be modified with the other. For example, Essigmann et al. does not suggest that the formation of UDP-SQ by SQD1 should be modified to include the formation of SQDG by sqdX. Vice versa, Guler et al. does not suggest that the formation of SQDG by *sqdX* should be modified to include the formation of UDP-SQ by *SQD1*. As the Applicants' have argued repeatedly, the Examiner has never pointed to any statements within either reference to suggest any modification to create the Applicants' claimed embodiment.

c. There Is No Expectation Of Success

A proper analysis under 35 U.S.C. § 103(a) requires that a combination of references must provide a reasonable expectation of success should the claimed combination be carried out. *MPEP* § 2143.02. Moreover, "both the suggestion and reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck,* 20 USPQ.2d 1438, 1442, 947 F.2d 488 (Fed. Cir. 1991). Essigmann et al., when read in view of teaching reference Guler et al. (as suggested by the Examiner) both do not provide any explicit suggestions that the Applicants' claimed embodiment would, in fact, work[19]. The same is true for Benning, Toth et al., and Bevan et al.

The Examiner, instead, simply offers personal interpretations of passages within the cited art in order to "fabricate an expectation of success", for example:

> One of ordinary skill in the art would have had a reasonable expectation of success since Essigmann et al. outlines the pathway for SQDG production and production of a product using recombinant enzymes in lieu of chemical synthesis is routinely performed.

Final Office Action Mailed Nov.26, 2001.

The Examiner also fails to reflect Guler's prophetic context, for example:

> Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to make SQDG with the polypeptide encoded by *sqdX* of Guler et al.

Office Action Mailed 05/09/01 pg 8 and Final Office Action Mailed 11/26/01, pg 3. In making this conclusion, the Examiner ignores the underlined hypothetical context from the relied upon passage:

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[19] The expectation of success must come from the prior art and explicitly predict that the process recited in the claims would work. *In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988).

> ... *SQDG1* ... genes encode highly conserved proteins with similarity to sugar-nucleotide-modifying enzymes which are proposed to be involved in the biosynthesis of the UDP-sulfoquinovose headgroup donor for sulfolipid biosynthesis ... [and] ... *sqdX*... sequence similarity to glycosyltransferases strongly suggests that *sqdX* encodes the sulfolipid synthase catalyzing the transfer of sulfoquinovose from UDP-sulfoquinovose onto a suitable acceptor, presumably diacylglycerol.

Guler et al., pg 545 ¶ 1 [emphasis added]. Guler et al. is clearly speculating and, as such, must be interpreted as "obvious to try" which does not rise to the statutory level of 35 U.S.C. § 103(a)[20]. Since an expectation of success is required to be explicitly present in a cited reference the Examiner's argument fails.

4. Rejection Under 35 USC § 103(a) Over Benning and Essigmann et al., in view of Toth et al. in further view of Bevan et al., in further view of Comai et al.

The Applicants request that all arguments presented in Section VII(A)(3)(a)(v), Section VII(A)(3)(b) and Section VII(A)(3)(c) be herein incorporated by reference. Further, Comai et al. adds nothing to fill the deficiencies of Benning, Essigmann et al., Toth et al., and Bevan et al. identified above. Specifically, Comai et al. discloses no nucleic acid sequences and is limited to plasmids containing a CaMV 35S-enhanced mannopine synthase promoter; Consequently, Claims 32-34 are not obvious because the independent Claim 26 is not obvious.

B. The Teaching References Add Nothing

The many teaching references asserted by the Examiner also do not teach any peptide encoded by SEQ ID NO:6 that converts UDP-Glc into UDP-SQ or any peptide encoded by SEQ ID NO:1 or SEQ ID NO:3 cDNA that converts UDP-SQ into SQDG. For example, McNally et al. examines the expression of myosin subtypes; Bidney et al. discloses no relevant nucleic acid sequences and is limited to binary vector plasmids; Dong et al. discloses no relevant nucleic acid sequences and is limited to plasmids containing cytochrome P450 synthase cDNA; Yue et al. discloses no relevant nucleic acid sequences and is limited to plasmids containing mammalian SR protein kinase DNA; Kovach et al. discloses no relevant nucleic acid sequences and is limited to pBBR1MCS plasmids that confer antibiotic resistance; and Bishop et al. is limited to plasmids

[20] "Of course, an 'obvious to try' standard is not a legitimate test of patentability." *American Hospital Supply Corp. v. Travenol Laboratories, Inc.*, 745 F.2d 1, 223 USPQ 577 (Fed. Cir. 1984)

containing Hepatitis B nucleic acids. All these references were fully analyzed and discredited in the Applicants' Response(s) mailed on either July 26, 2004 or March 21, 2005.

It is respectfully submitted that the Examiner's combination of references is really a house of cards. There is nothing specific in the entire collection of references which teaches the presently claimed embodiment of the invention. Citing random references teaching biotechnology in other systems add nothing to the Examiner's analysis. The question is whether the art teaches transfection with the *two particular genes* set forth in the claims. The Examiner's argument is equivalent to citing the Maniatis treatise as prior art. The Board knows its record of published decisions which point out that general protocols are of no moment when the claims specify particular genes.

The Board should now realize that a primary factor required to establish a *prima facie* case of obviousness is absent (i.e., a teaching of all the claim elements). The Applicants respectfully request that the claims now be passed into allowance.

C. The Examiner Has Unlawfully Ignored a Declaration Establishing That One Skilled in the Art Understand That Essigmann et al. And Guler et al. Do Not Teach An SQDG Biosynthetic Pathway

In response to Final Office Action of 11/26/01 a declaration by Dr. Christoph Benning was submitted to establish the skill in the art. (see Appendix B) Specifically, the Benning Declaration teaches that, in the art of genetic engineering, the Essigmann et al. and Guler et al. publications are insufficient to teach one having ordinary skill in the art to make and use a biosynthetic pathway comprising SEQ ID NO:6 (i.e., Essigmann et al. and Guler et al. are not enabling references)[21].

The Examiner fails to mention the Benning Declaration within the subsequent Office Action mailed 05/23/02 subsequent to the Applicant's Request For Continuing Examination. In essence, the Examiner has IGNORED submitted evidence by the Applicants. This act amounts to a summary dismissal of the declaration. The Examiner has failed to accord proper deference to the statements of one skilled in the art as required under the law.

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[21] In order to render a claimed apparatus or method obvious under Section 103, the prior art must enable one skilled in the art to make and use the apparatus or method. *Beckman Instruments, Inc. v. LKB Produkter AB,* 892 F.2d 1547, 1551 (Fed. Cir. 1997).

In the submitted Benning Declaration, a factual basis is set forth for the conclusion that Essigmann et al. is understood by one skilled in the art not to teach a successful recombinant SQDG biosynthetic pathway. It is established that Essigmann et al. does not disclose any insight into the expression of an active SQD1 protein. For example, "The Essigmann paper is completely silent on how the enzyme protein works, whether the enzyme must be an active (i.e., functioning) protein, how one would express (i.e., recombinantly) and isolate such an active protein, or how one would assay its activity". See Benning Declaration, ¶ 3. It is also established that Figure 1 in the Essigmann et al. publication does not provide sufficient disclosure to use recombinant proteins to produce either UDP-SQ and/or SQDG. For example, "Figure 1 merely depicts a "model of the sugar-nucleotide pathway for sulfolipid biosynthesis" without providing direction as to the appropriate buffer conditions, sulfite, and recombinant enzymes required ...". See Benning Declaration, ¶ 4.

The Benning Declaration also sets forth a factual basis for the conclusion that Guler et al. is understood by one skilled in the art not to teach a successful recombinant SQDG biosynthetic pathway. For example, "The reference is completely silent on the use of a first and second recombinant peptide (i.e., *SQD1* and *sqdX* respectively) in a biochemical method to produce UDP-sulfoquinovose and covert it to SQDG." See Benning Declaration ¶ 5.

These statements of fact must be addressed directly by the Examiner in order to maintain a rejection of the claims. *In re Alton*, 37 U.S.P.Q.2d 1578 (1996), *In re Meng*, 492 F.2d 843, 849 (CCPA 1974). In *Alton*, the Examiner summarily dismissed a declaration providing factual support for a conclusion that a claimed composition of matter was adequately described in the specification. The Court stressed that the declaration contained factual statements to support its conclusion and that it is the burden of the Examiner to address these factual statements and explain why they are incorrect or unpersuasive. A factually supported declaration cannot be summarily dismissed.

The Applicants submit that the Benning Declaration, alone, is sufficient evidence to overcome the Examiner's present obviousness rejection. Consequently, the Applicants respectively request the Board pass the present claims into allowance.

D. Conclusion

Appellants submit that, with due consideration to all these factors discussed above, the patentability of Claims 1, 13, and 15-40 is evident. None of the cited references teach any biosynthetic method to produce SQDG or even disclose an enabling combination of references teaching nucleic acids that would create the Applicants' claimed embodiment. The Examiner has also ignored an evidentiary Declaration submitted by one having ordinary skill in the art to establish that Essigmann et al. and Guler et al. are not enabling references.

The Examiner continues to assert an increasing number of teaching references directed to irrelevant gene expression techniques. Additionally, the Examiner has dropped several Benning/Essigmann et al. combinations, only to recombine them with new and equally ineffective references.

For these reasons, the Applicants now appeal because it appears the Examiner has taken an arbitrary and intransigent postion. It is submitted that the Examiner's rejections of Claims 1, 13,and 15-40 were erroneous, and reversal of these rejections is respectfully requested.

Respectfully submitted,

Medlen & Carroll, LLP

Dated: October 19, 2005

Peter G. Carroll
Registration No. 32, 837
Attorney for Appellant

VIII. CLAIMS APPENDIX

1. A method, comprising:

a) providing:

i) uridine-5'-diphosphoglucose;

ii) sulfite;

iii) an isolated first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6; and

iv) an isolated second peptide encoded by a nucleic acid selected from the group consisting of SEQ ID NO:1 and the cDNA corresponding to SEQ ID NO:3;

b) reacting said uridine-5'-diphosphoglucose with said first peptide and said sulfite under such conditions that uridine-5'-diphosphosulfoquinovose is generated; and

c) treating said uridine-5'-diphosphosulfoquinovose with said second peptide under conditions such that sulfoquinovose diacylglycerol is generated.

13. A method, comprising:

a) providing:

i) uridine-5'-diphosphoglucose;

ii) sulfite; and

iii) an isolated peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6; and

b) reacting said uridine-5'-diphosphoglucose with said peptide and said sulfur donor under such conditions that uridine-5'-diphosphosulfoquinovose is generated.

15. A method, comprising:

a) providing:

i) uridine-5'-diphosphoglucose;

ii) sulfite;

iii) the nucleic acid sequence set forth in SEQ ID NO: 6; and

iv) a host cell;

b) transfecting said host cell with said nucleic acid under conditions such that a peptide is expressed;

c) isolating said expressed peptide; and

d) reacting uridine-5'-diphosphoglucose with said peptide of step (c) and said sulfite under conditions such that uridine-5'-diphosphosulfoquinovose is produced.

16. A method, comprising:

a) providing:

i) uridine-5'-diphosphosulfoquinovose;

ii) diacylglycerol;

iii) a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and the cDNA corresponding to SEQ ID NO:3; and

iv) a host cell

b) transfecting said host cell with said nucleic acid under conditions such that a peptide is expressed;

c) isolating said expressed peptide; and

d) reacting uridine-5'-diphosphosulfoquinovose with said peptide of step (c) and said diacylglycerol under conditions such that sulfoquinovosyl diacylglycerol produced.

17. A method, comprising:

a) providing:

i) a first vector comprising the nucleic acid sequence set forth in SEQ ID NO: 6;

ii) a second vector comprising the nucleic acid sequence set forth in SEQ ID NO: 1; and

iii) a host cell;

b) transfecting said host cell with first and second vectors, thereby creating a transformed host cell, under conditions such that sulfoquinovosyl diacylglycerol is produced by said transformed host cell.

18. The method of Claim 17, wherein said host cell, prior to said transfecting of step (b) does not produce sulfoquinovosyl diacylglycerol.

19. The method of Claim 18, wherein said host cell is a bacterial host cell.

20. The method of Claim 19, wherein said bacterial host cell is E. coli.

21. The method of Claim 17, wherein said first and second vectors are plasmids conferring different antibiotic resistance on said transformed host cell.

22. The method of Claim 17, wherein said host cell, prior to said transfecting of step (b) produces less sulfoquinovosyl diacylglycerol than said transformed host cell.

23. The method of Claim 22, wherein said host cell is a plant host cell.

24. The method of Claim 23, wherein said plant host cell is derived from a monocotyledonous plant.

25. The method of Claim 23, wherein said plant host cell is derived from a dicotyledonous plant.

26. A method, comprising:

a) providing:

i) a first vector comprising the nucleic acid sequence set forth in SEQ ID NO: 6;

ii) a second vector comprising the nucleic acid sequence corresponding to the cDNA of the sequence set forth in SEQ ID NO: 3; and

iii) a host cell;

b) transfecting said host cell with first and second vectors, thereby creating a transformed host cell, under conditions such that sulfoquinovosyl diacylglycerol is produced by said transformed host cell.

27. The method of Claim 26, wherein said host cell, prior to said transfecting of step (b) does not produce sulfoquinovosyl diacylglycerol.

28. The method of Claim 27, wherein said host cell is a bacterial host cell.

29. The method of Claim 28, wherein said bacterial host cell is E. coli.

30. The method of Claim 26, wherein said first and second vectors are plasmids conferring different antibiotic resistance on said transformed host cell.

31. The method of Claim 26, wherein said host cell, prior to said transfecting of step (b) produces less sulfoquinovosyl diacylglycerol than said transformed host cell.

32. The method of Claim 31, wherein said host cell is a plant host cell.

33. The method of Claim 32, wherein said plant host cell is derived from a monocotyledonous plant.

34. The method of Claim 32, wherein said plant host cell is derived from a dicotyledonous plant.

35. The method of Claim 1, further comprising the step of isolating said sulfoquinovose diacylglycerol generated in step (c).

36. The method of Claim 13, further comprising the step of isolating said uridine-5'-diphosphosulfoquinovose generated in step (b).

37. The method of Claim 15, further comprising the step of isolating said uridine-5'-diphosphosulfoquinovose produced in step (d).

38. The method of Claim 16, further comprising the step of isolating said sulfoquinovosyl diacylglycerol produced in step (d).

39. The method of Claim 17, further comprising the step of isolating said sulfoquinovosyl diacylglycerol produced in step (b).

40. The method of Claim 26, further comprising the step of isolating said sulfoquinovosyl diacylglycerol produced in step (b).

IX. EVIDENCE APPPENDIX

THE DECLARATION OF DR. CHRISTOF BENNING

PATENT
Attorney Docket No. **MSU-04769**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Christoph Benning, *et al.*
Serial No.: 09/709,020 Group No.: 1652
Filed: 11/08/2000 Examiner: Y. Pak
Entitled: **Compositions and Methods For The Synthesis And Subsequent Modification Of Uridine-5'-Diphosphosulfoquinovose (UDP-SQ)**

DECLARATION OF DR. CHRISTOPH H. BENNING PURSUANT TO 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: 3/11/05 By: Traci E. Light

I, Dr. Christoph H. Benning, under penalty of perjury, state that:

1. I am a joint inventor of the subject matter claimed in the above captioned United States Patent Application.

2. I have reviewed the following journal articles:

A. "Essigmann *et al.*, "Prediction of the Active-Site Structure and NAD^+ Binding in SQD1, a Protein Essential for Sulfolipid Biosynthesis in *Arabidopsis*," *Arch. Biochem. & Biophys.*, 369: 30-41 (1999)(hereinafter "the Essigmann paper"); and

B. "Güler *et al.*, A Cyanobacterial Gene, *sqdX*, Required for Biosynthesis of the Sulfolipid Sulfoquinovosyldiacylglycerol," *J. Bacteriol.*, 182(2): 543-45 (2000)(hereinafter "the Güler paper").

3. I am a co-author of the Essigmann. This paper describes experiments conducted to determine the structure of the active site of the SQD1 enzyme protein. The Essigmann paper is completely silent on how the enzyme protein works, whether the enzyme must be an active (*i.e.* functioning) protein, how one would express (*i.e.* recombinantly) and

isolate such an active protein, or how one would assay its activity. Unlike the present invention, the Essigmann paper does not disclose all of the four *critical* elements of the enzymatic biosynthesis of UDP-sulfoquinovose: active SQD1 enzyme, UDP-glucose, sulfite, and the appropriate buffer conditions. Furthermore, the discussion of a "sulfur donor" is made within the context of a chemical synthesis scheme. The papers cited as references 43 and 44 in support of the discussion of sulfite all refer to chemical synthesis reactions, not enzymatic biosynthesis methods.[1] The Essigmann paper only suggests a model of how a plant may make sulfite. The paper does not disclose that sulfite is "the" sulfur donor in an enzymatic biosynthesis method to produce UDP-sulfoquinovose by using SQD1, UDP-glucose, sulfite, and the appropriate buffer conditions.

4. With respect to Figure 1 of the Essigmann paper (and its corresponding text), the figure is completely silent on the use of a first and second recombinant (*i.e.* SQD1 and *sqdX* respectively) in a biochemical method to produce UDP-sulfoquinovose and SQDG. Figure 1 merely depicts a "*model* of the sugar-nucleotide pathway for sulfolipid biosynthesis" without providing direction as to the appropriate buffer conditions, sulfite, and recombinant enzymes required for a biochemical method to produce UDP-sulfoquinovose and SQDG as claimed by the present invention. There is also no suggestion of such an approach in the text of the Essigmann paper.

5. I am a co-author of the Güler paper. This paper describes the disruption and restoration of sulfolipid production in cyanobacteria by removal and replacement of the *sqdX* gene. The reference is completely silent on the use of a first and second recombinant peptide (*i.e.* SQD1 and *sqdX* respectively) in a biochemical method to produce UDP-sulfoquinovose and convert it to SQDG. The reference neither discusses, nor suggests, the *critical* elements of the enzymatic biosynthesis of UDP-sulfoquinovose and its conversion to SQDG: active SQD1 enzyme, UDP-glucose, sulfite (as the sulfur donor), active sqdX (or AtSQDX-1) enzyme, diacylglycerol, and the appropriate buffer conditions.

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[1] Moreover, the paper cited as reference 41 only discusses sugar modifying enzymes in general and mentions UDP-4-keto-5,6-glucoseen (*i.e.* not UDP-SQ or SQDG). Reference 41 is also completely silent with respect to sulfite.

6. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Dated: 11/8/02

Christoph H. Benning

X. RELATED PROCEEDINGS APPENDIX

(No attachments are required for this Brief)